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Cant  
D1

(i) an effective amount of at least one supplement selected from the group consisting of [a growth factor, an antibody, a polynucleotide or oligonucleotide,] a cytotoxin or cell proliferation inhibiting compound, an osteogenic [or] compound, a cartilage inducing compound, an [antimicrobial composition, an analgesic] antibiotic, an anesthetic, an anticoagulant compound, an anti-inflammatory compound, [a cytokine, a chemotherapeutic drug, a hormone, an interferon, a lipid, a polysaccharide,] a cardiovascular drug, a protease inhibitor, [a proteoglycan,] and a steroid [, a vasoconstrictor, a vasodilator, a vitamin, a nutritional mineral,] ; and

(ii) a biocompatible tissue sealant composition comprising fibrinogen, or a derivative or metabolite thereof selected from the group consisting of fibrinopeptide A and fibrinopeptide B, in an amount which forms a fibrin matrix;  
wherein said fibrinogen, or said derivative or metabolite thereof, will form a fibrin matrix when hydrated under suitable conditions, and  
further wherein said supplement is delivered from said fibrin matrix into the external environment of use for a sustained period, and  
further wherein said effective amount of said supplement is greater than the amount which is soluble in said fibrin matrix.

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17. (Twice amended) The delivery system of claim [14] 12, 34 or 36, wherein said supplement is introduced into said biocompatible tissue sealant composition prior to formation of said fibrin matrix as an emulsion of said supplement in a carrier liquid or component of said fibrin matrix.

18. (Twice amended) The delivery system of claim [14] 12, 34 or 36, wherein said supplement interacts with said fibrin matrix and so retards degradation of said fibrin matrix in said external environment of use, thereby permitting localized, sustained-release of said supplement.

19. (Twice amended) The delivery system of claim [14] 12, 34 or 36, wherein said supplement is present in said fibrin matrix in solid form.

20. (Twice amended) The delivery system of claim 19, wherein said supplement is introduced into said biocompatible tissue sealant composition [in] prior to formation of said fibrin matrix as a solution of said supplement dissolved in a carrier liquid, said carrier liquid having a higher rate of dissolution or diffusion in said fibrin matrix than said [composition] supplement contained therein, so that said supplement is deposited within [said] the resulting fibrin matrix as a solid precipitate.

24. (Amended) The delivery system of claim [13] 12, wherein said supplement is a cytotoxin or cell proliferation inhibiting compound and said [tissue] environment of use is a neoplastic or hyperproliferative lesion of a patient and tissue adjacent thereto.

25. (Amended) The delivery system of claim [12] 36, wherein said supplement is a growth factor selected from the group consisting of: fibroblast growth factors; platelet-derived growth factors; insulin-binding growth factors; epidermal growth factors; transforming growth factors; cartilage-inducing factors; osteoid-inducing factors; osteogenin [and other]; bone

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growth factors; bone morphogenetic growth factors; collagen growth factors; heparin-binding growth factors; cytokines; interferons; and hormones [and biologically active derivatives of said growth factors].

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26. (Amended) The delivery system of claim [12] 36, wherein said supplement is an osteogenic protein or cartilage inducing [compound] protein selected from the group consisting of: cartilage-inducing factors; osteoid-inducing factors; osteogenin [and other] ; bone growth factors which modulate the proliferation, migration and/or attraction of progenitor bone cells; bone morphogenetic growth factors; and demineralized bone matrix [; and biologically active derivatives of said compounds].

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28. (Amended) The delivery system of claim [12] 34, wherein said supplement is a polynucleotide or an oligonucleotide.

29. (Amended) The delivery system of claim [12] 34 or 36, wherein said supplement is an antimicrobial [compound].

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30. (Amended) The delivery system of claim 12 , 34 or 36, wherein said biocompatible tissue sealant composition further comprises thrombin [or other activator of fibrin formation].

31. (Amended) The delivery system of claim 12 , 34 or 36, wherein said biocompatible tissue sealant composition further comprises Factor XIII.

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C4  
cont

32. (Amended) The delivery system of claim 12, 34 or 36, wherein said biocompatible tissue sealant composition further comprises  $\text{Ca}^{++}$ .

(Please add the following new claims 34-37.)

~~34.~~ A supplement delivery system comprising:

(i) an effective amount of at least one supplement selected from the group consisting of an analgesic, an antifungal compound, an anti-angiogenic compound, an antifibrinolytic compound, an antimicrobial compound, an antiparasitic agent, an antiseptic, an antiviral compound, a chemotherapeutic drug, a lipid or liposome, an oligonucleotide or polynucleotide, a polysaccharide, a vasoconstrictor, a vasodilator, a vitamin, a nutritional supplement and a mineral; and

(ii) a biocompatible tissue sealant composition comprising fibrinogen, or a derivative or metabolite thereof selected from the group consisting of fibrinopeptide A and fibrinopeptide B, in an amount which forms a fibrin matrix; wherein said fibrinogen, or said derivative or metabolite thereof, will form a fibrin matrix when hydrated under suitable conditions, and further wherein said supplement is delivered from said fibrin matrix into the external environment of use for a sustained period, and further wherein said amount of said supplement is greater than the amount which is soluble in said fibrin matrix.

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35. The delivery system of claim 12, 34 or 36, further comprising at least one agent that stabilizes said fibrin matrix and so retards degradation thereof in said external environment of use.

36. A supplement delivery system comprising:

(i) an effective amount of at least one supplement selected from the group consisting of a growth factor, an osteogenic protein, a cartilage inducing protein, an antimicrobial protein, an anticoagulant protein, an antibody, an anti-angiogenic protein, a proteoglycan, a protease inhibitor, a polypeptide, an antifibrinolytic protein, an interferon, a hormone and a cytokine; and

(ii) a biocompatible tissue sealant composition comprising fibrinogen, or a derivative or metabolite thereof selected from the group consisting of fibrinopeptide A and fibrinopeptide B, in an amount which forms a fibrin matrix;  
wherein said fibrinogen, or said derivative or metabolite thereof, will form a fibrin matrix when hydrated under suitable conditions, and  
further wherein said supplement is delivered from said fibrin matrix into the external environment of use for a sustained period.

37. The delivery system of claim 12, 34 or 36, wherein at least one protein is a recombinantly-produced protein.

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